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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/237,291	01/25/1999	JUDY CAROL YOUNG	SYS-2068	9391

1095 7590 05/06/2005

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
MONTANARI, DAVID A	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/237,291	YOUNG ET AL.	
	Examiner	Art Unit	
	David Montanari	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/18/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-20,23-27,31-34,37-43,46-50 and 52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-20,23-27,31-34,37-43,46-50 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This application has been transferred to David Montanari, Ph.D., AU 1632.

2. Applicant's amendment filed 2/18/2005 have been entered.

The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f). The specification sites Cwirla et al. as teaching a mimetic of thrombopoietin. However, Cwirla et al. only teaches one such mimetic, AF13948 . This is an improper incorporation by reference because the mimetic is essential to the implementation of the claims. Applicant is permited only to amend the specification to add the name of the mimetic.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18, 23, 37, and 48-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 18, 23, 37, and 48-50 are drawn to methods of obtaining pluripotent hematopoietic stem cells cultured with RetroNectin™. RetroNectin™ is a commercially available form of fibronectin produced by Takara Shuzo Co. Ltd., of Otsu Shigi, Japan. The claimed invention requires RetroNectin™ for the practice and implementation of the invention. The specification fails to disclose a readily available and reproducible source for RetroNectin™ for the life of any issuing patent. There is no guarantee that RetroNectin will be so available. Thus, applicant needs to ensure that RetroNectin is available to the public for the life of the patent or delete this reference from the claims. Further, there is no disclosure that indicates the components in RetroNectin such that the skilled artisan could repeat the invention. The specification offers no guidance on what is RetroNectin or how to make the compound. Therefore, the skilled artisan would need to engage in an undue amount of experimentation without a predictable degree of success to implement claims 18, 23, 37, and 48-50.

Claim 43 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 43 is drawn to a mimetic of thrombopoietin (TPO). The

specification teaches that the TPO mimetic is taught in a reference (Cwirla et al. Science, 1997, Vol. 276 pgs. 1696-1699). Sufficient numbers of mimetics have not been described so that the skilled artisan could envision other mimetics. Thus, applicant cannot convey the invention, and one cannot convey what one has not invented.

The MPEP 2163.02 states:

> Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., Pfaff v. Wells Electronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Regents of the University of California v. Eli Lilly, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it"). The subject matter of the claim need not be described literally (i.e., using the same terms or in haec verba) in order for the disclosure to satisfy the description requirement. If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.

It is maintained that the present specification provides no such reasonable clarity to those skilled in the art that Applicant was in possession of the claimed invention. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18-20,23-27,31-34,37-43,46-50 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nolta et al. (Blood, 1995, Vol. 86 pgs. 101-110), and further in view of Young et al. (Blood, 1996, Vol. 88 pgs. 1619-1631), and Kuga et al. (Human Gene Therapy, 1997, Vol. 8 pgs. 1901-1910).

Nolta et al. teach pluripotent $CD34^+$ Thy-1 Lin^- cells cultured with and without stromal support in the presence of interleukin-3 (IL-3), interleukin-6 (IL-6), and stem cell factor (SCF) (pg. 102 col. 1 parag. 4 lines 9-13), and further transduced with a retroviral vector comprising the bacterial *neo* gene (pg. 101 col. 2 parag. 2 lines 1-2). Nolta et al. further teach that stromal-derived cytokines, leukemia inhibitory factor (LIF), and flk-2 (e.i, flt3) have been shown to stimulate division of primitive hematopoietic cells and may be potentially used in the absence of stromal cells to increase cycling of quiescent hematopoietic progenitor cells to allow retroviral integration (pg. 109 col. 2 parag. 1 lines 1-9).

Young et al. teach pluripotent $CD34^+$ Thy-1 Lin^- cells cultured with stromal support and thrombopoietin (TPO, an mpl ligand) and c-kit ligand (pg. 1620 col. 2 parag. 1). Young et al. continue to teach that TPO stimulated division of $CD34^+$ Thy-1 Lin^- cells, and further enhanced division when combined with IL-3 or c-kit ligand (pg. 1621 Fig. 1).

Kuga et al. teach $CD34^+$ cells cultured with IL-3/IL-6/SCF and transduced with a retroviral vector comprising the glutathione-S-transferase π gene with and without the

presence of a recombinant fibronectin fragment (pg. 1903 col. 1 parag. 2 bridge col. 2 1st full parag.). Kuga et al. continue that fibronectin improved transduction efficiency of the glutathione-S-transferase π gene compared to not using the fibronectin and only IL-3/IL-6/SCF ligands (pg. 1904 col. 2 parag. 4 and Table 1).

Motivation is provided by the art teaching that pluripotent $CD34^+$ Thy-1 Lin^- cells have enhanced transduction with retroviral vectors when cultured with IL-3, IL-6, and SCF, and may have further enhanced transduction when cultured with flk-2, and LIF as taught by Nolta. Further motivation is provided by Young teaching pluripotent $CD34^+$ Thy-1 Lin^- cells have increased division when cultured with TPO, and Kuga teaching that $CD34^+$ cells have improved transduction efficiency from retroviral vectors when cultured with fibronectin.

Thus, it would have been obvious to the ordinary artisan at the time of filing to culture pluripotent $CD34^+$ Thy-1 Lin^- cells in the presence of mpl ligand, flt-3 ligand and fibronectin with or without, IL-3, IL-6, LIF, or c-kit ligand and further transduced cultured cells with a retroviral, adenoviral, or adeno-associated viral vector given the teachings and motivations of Nolta to culture pluripotent $CD34^+$ Thy-1 Lin^- cells without stromal support and IL-3, IL-6 and to use flk-2 or LIF to improve cellular division, in view of the teachings and motivation of Young to culture pluripotent $CD34^+$ Thy-1 Lin^- cells with TPO to improve cellular division and further in view the teachings and motivations of Kuga teaching pluripotent $CD34^+$ cells cultured with fibronectin have improved viral vector transduction. Thus, the cited prior art provides the requisite teachings, suggestions, and motivation to make and use the claimed genetically modified mouse.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Montanari whose telephone number is 1-571-272-3108. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 1-571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 1-571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800/630

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